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Program/Abstract # 393
Vascular function and growth is differentially regulated by fetal and placental PKBalpha/Akt1 in a gene dosage dependent manner: Non-invasive dynamic contrast enhanced MRI
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Program/Abstract # 394
Disruptions in reelin signaling alter mammary gland development
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The reelin signaling pathway has been examined primarily for its role in promoting the correct positioning of cortical, cerebellar, and hippocampal neurons during brain development. However, disruptions in the reelin signaling pathway also affect the development of non-neural structures. We have examined the expression and activity of components of the reelin signaling pathway in the developing mammary gland. During embryogenesis, Dab1, an intracellular adaptor protein that is activated in response to reelin signaling, is expressed in the developing mammary bud, while reelin itself is expressed in the overlying epithelium. In the mature gland, Dab1 is expressed in mammary epithelial cells lining the mammary ducts, while reelin is expressed in the periductal stroma. Disrupting reelin signaling by inactivating either the reelin or the *Dab1* gene induces alterations in the development of the ductal network, including significant retardation in ductal growth and abnormal ductal branching and cavitation. We have also found that isolated mammary epithelial cells decrease their migration in response to the presence of reelin in vitro. These observations support a role for reelin signaling in non-neural tissues, specifically in regulating the migration of mammary epithelial cells and in the development of the mammary gland.

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Program/Abstract # 395
Cell-autonomous role of hedgehog signaling in notochord and intervertebral disc development
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The vertebrate notochord is a transient embryonic structure that serves as a signaling center in the midline of the developing early embryo. In later embryogenesis, the notochord becomes discontinuous and we have shown that it derives the nucleus pulposus located in the center of the intervertebral discs. Although hedgehog signaling has been well studied over the past decades, the role of hedgehog signaling in the notochord and nucleus pulposus is still unclear. Here we show that hedgehog signaling is required not only for maintaining notochord structure but for forming the nucleus pulposus. In this study we abolished a co-receptor of hedgehog signaling, *smoothened* (*smo*), to remove all hedgehog signaling in the notochord using a tissue-specific cre allele (*Shhcre*). Upon loss of hedgehog signaling, notochord formation was initiated but failed to differentiate to make the notochord sheath, which normally surrounds the notochord. Failure to form a notochord sheath resulted in aberrant nucleus pulposus formation. We showed that *Noto* and *Foxa2* expression were decreased in caudal mutant notochord. Interestingly, *Sonic hedgehog* (*Shh*) expression was also decreased in the entire notochord and floorplate during early embryonic development. *Shh* expression then became discontinuous in the caudal mutant notochord during later development. Our data indicates that hedgehog signaling plays a cell-autonomous role in maintaining *Shh* expression in both the notochord and floorplate. In addition, these results demonstrate that hedgehog signaling is required for formation of the notochord sheath and intervertebral discs.

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Program/Abstract # 396
Gpi-anchored proteins regulate cell signaling and cell intercalation in growth plate cartilage
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Proteins that are localized to the cell surface via glycosylphosphatidylinositol (Gpi) linkages have been proposed to regulate cell signaling and cell adhesion events involved in tissue patterning. Here we demonstrate that during skeletal development Gpi-anchored proteins play limited, focal roles in chondrogenesis. Conditional deletion of *Piga*, an essential enzyme in the Gpi-biosynthetic pathway, in the lateral plate mesoderm results in limbs that display chondrodysplasia. Analysis of mutant and mosaic *Piga* cartilage revealed two independent cell autonomous defects. First, loss of *Piga* function interferes with signal reception by cells and results in delayed chondrocyte maturation. Second, the proliferative chondrocytes, while present, fail to flatten and arrange into columns of clones as in wildtype tissue. We present evidence that the abnormal organization of mutant proliferative chondrocytes results from errors in cell intercalation following cell division. Consistent with the known relationship between cell polarity and cell intercalation, we additionally show that Gpi-anchored proteins regulate cell polarity in other tissues. Collectively, our data suggest that the distinct morphological features of the proliferative chondrocytes result from regulated cell polarity that is controlled independent of chondrocyte maturation.

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Program/Abstract # 397
Gene-switching, cell-switching and cell-reprogramming during metamorphosis in *Xenopus laevis*
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Metamorphosis is characterized by growth, death and remodeling programs during the 8days of climax when the *Xenopus laevis* tadpole is converted to a frog. All of these varied programs are controlled by